REMARKS

The present application is directed to isolated proteins comprising a fragment of a NC1 region of a collagen protein. The proteins have the ability to inhibit angiogenesis.

Claims 52-73 are pending in the above-identified patent application. No new matter is introduced by the amendments. Applicants respectfully assert that the amendments to the claims do not diminish the scope of the invention as originally claimed. Based on the foregoing amendments and the following remarks, Applicants respectfully request allowance of all of the pending claims.

Rejections under 35 U.S.C. §112, first paragraph

Claims 52-73 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office Action indicates that there is insufficient guidance regarding which fragments, of what size, and from what region, within the C-terminus of a collagen molecule would be predicted to inhibit endothelial cell proliferation. The claims have been amended to indicated that the invention is directed to "an isolated protein comprising **a fragment of a NC1 region of a collagen protein**, wherein the fragment inhibits angiogenesis". In light of these amendments, Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. §112, second paragraph

Claims 53 and 64 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office Action indicates that the terminology "non-fibrillar collagen protein" renders these claims vague and indefinite. Claim 53 is dependent upon Claim 52 and Claim 64 is dependent upon Claim 63. In light of the amendments to claims 52 and 64, which now refer to proteins comprising "a fragment of a NC1 region of a collagen protein", Applicants respectfully request that the rejection be withdrawn.

Rejection of Claims 52-62 As Being Unpatentable Over U.S. Patent No. 5,854,205

Claims 52-62 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-7 and 17-23 of U.S. Patent No. 5,854,205. The Office Action states that "although the conflicting claims are not identical, they

are not patentably distinct from each other because the only difference between the two inventions is the scope of the claimed endostatin."

Applicants respectfully disagree with the Examiner's position that amended Claims 52-62 are obvious in view of the above recited patent. However, to advance prosecution, Applicants will file a terminal disclaimer in compliance with 37 C.F.R. §3.37(b) once the claims are indicated to be allowable. Applicant respectfully requests reconsideration and withdrawal of this ground of rejection.

Rejection of Claims 52-62 As Being Unpatentable Over co-pending Application No. 09/315,689

Claims 52-62 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-8, 15-17 and 19-20 of co-pending Application No. 09/315,689. The Office Action states that "although the conflicting claims are not identical, they are not patentably distinct from each other because the only difference between the two inventions is the scope of the claimed endostatin."

Both the present application and Application No. 09/315,689 are pending. Allowable subject matter, notwithstanding the provisional obviousness-type double patenting rejection, has not been indicated in either application. Where a provisional rejection under the judicially created doctrine of obvious type double patent is made between two applications, MPEP §804(I)(B) states that "if the 'provisional' double patenting rejection in one application is the only rejection remaining in that application, the Examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the 'provisional' double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent." Therefore, it is not evident which of the pending applications will become allowable first, and any action to this provisional rejection is premature.

In light of the above, Applicants respectfully submit that Claims 52-55, 57-66 and 68-73 are allowable, and a Notice of Allowance is courteously solicited. The foregoing is submitted as a full and complete response to the Office Action mailed December 19, 2000. The Examiner is invited and encouraged to contact the undersigned attorney of record if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted,

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Amendments to the Claims Showing Changes Made

In accordance with 37 C.F.R. 1.12(c), the following versions of the claims as rewritten by the foregoing amendment show all of the changes made relative to the previous versions of the claims.

Please amend the claims as follows:

52.(Amended) An isolated [Isolated endostatin] protein [, wherein the protein is] comprising a fragment of a NC1 [C-terminal non-collagenous] region of a collagen protein, [and] wherein the [endostatin protein is further characterized by its ability to inhibit] fragment inhibits angiogenesis.

53.(Amended) The [endostatin] protein of Claim 52, wherein the [endostatin] protein is a fragment of a non-fibrillar collagen protein.

54.(Amended) The [endostatin] protein of Claim 52, wherein the [endostatin] protein is a fragment of a collagen type XVIII protein.

55.(Amended) The [endostatin] protein of Claim 52, wherein the [endostatin] protein is a fragment of a collagen type XV protein.

57.(Amended) The [endostatin] protein of Claim 52, wherein the [endostatin] protein is produced recombinantly.

58.(Amended) The [endostatin] protein of Claim 52, wherein the [endostatin] protein is naturally occurring.

59.(Amended) The [endostatin] protein of Claim 52, wherein the [endostatin] protein is human.

60.(Amended) The [endostatin] protein of Claim 52, wherein the [endostatin] protein inhibits angiogenesis *in vivo*.

61.(Amended) The [endostatin] protein of Claim 52, wherein the [endostatin] protein inhibits angiogenesis *in vitro*.

62.(Amended) The [endostatin] protein of Claim 52, wherein the [endostatin] protein has an N-terminal amino acid sequence as shown in SEQ ID NO:1.

63.(Amended) A composition comprising, an endostatin protein combined with an angiostatin protein, wherein the endostatin protein is a fragment of a NC1 [C-terminal non-collagenous] region of a collagen protein, wherein the angiostatin protein is a fragment of a kringle region of plasminogen and wherein the endostatin protein and the angiostatin protein are further characterized by their ability to inhibit angiogenesis.